#### **PCT**

# WORLD INTELLECTUAL PROPERTY ORGANIZATION International Bureau



#### INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification <sup>6</sup> :		(11) International Publication Number: WO 99/33443
A61K 7/48, 7/00	A1	(43) International Publication Date: 8 July 1999 (08.07.99)
<ul> <li>(21) International Application Number: PCT/IL</li> <li>(22) International Filing Date: 17 December 1998 (</li> <li>(30) Priority Data: 122776 28 December 1997 (28.12.9</li> <li>(71) Applicant (for all designated States except US): DELABORATORIES LTD. [IL/IL]; Mitzpe Shaler Mobile Post Dead Sea (IL).</li> <li>(72) Inventors; and</li> <li>(75) Inventors/Applicants (for US only): MAOR, Zee Kalya, 90666 Dead Sea (IL). YEHUDA, Shau Mitzpe Shalem, 86983 Mobile Post Dead Sea (ID DASSI, Shlomo [IL/IL]; Hanerd 36, 96626 Jerus KOGAN, Assia [IL/IL]; Brazil 26, 96784 Jerusale (74) Agent: NOAM, Meir; P.O. Box 34335, 91342 Jerusale</li> </ul>	(17.12.9 (17.12.9 (17.12.9) (17.12.9) (18.12.9) (18.12.9) (18.12.9) (18.12.9) (18.12.9) (18.12.9) (18.12.9) (18.12.9) (17.12.9)	BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SZ, UG, ZW), Eurasian patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).  Published  With international search report.  Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.

(54) Title: A GEL COMPOSITION FOR SKIN CARE AND PROTECTION AND A METHOD FOR PREPARATION THEREOF

#### (57) Abstract

The present invention relates to a gel composition useful for skin care and protection comprising up to 80 % w/w Dead Sea water, hydrophobic and/or hydrophilic active agents, solubilizers, gelling agents or viscosity modifiers and water to complete up to 100 %. Preferably, the composition is a clear liquid gel. In the composition of the present invention the hydrophobic active agents may be vegetable oils, free fatty acids or vitamins, or any combination thereof and the hydrophilic active agent may be humectants,  $\alpha$ -hydroxy acids, anti irritant agents, plant extracts, moisturizing agents or hydrolyzed plant proteins or any combination thereof. The gel may further comprise antioxidants and fragrances. The present invention further relates to a method for the preparation of the said composition.

## FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AL	Albania	ES	Spain	LS	Lesotho	SI	Slovenia
AM	Armenia	FI	Finland	LT	Lithuania	SK	Slovakia
AT	Austria	FR	France	LU	Luxembourg	SN	Senegal
ΑU	Australia	GA	Gabon	LV	Latvia	SZ	Swaziland
AZ	Azerbaijan	GB	United Kingdom	MC	Monaco	TD	Chad
BA	Bosnia and Herzegovina	GE	Georgia	MD	Republic of Moldova	TG	Togo
BB	Barbados	GH	Ghana	MG	Madagascar	ТJ	Tajikistan
BE	Belgium	GN	Guinea	MK	The former Yugoslav	TM	Turkmenistan
BF	Burkina Faso	GR	Greece		Republic of Macedonia	TR	Turkey
BG	Bulgaria	HU	Hungary	ML	Mali	TT	Trinidad and Tobago
BJ	Benin	IE	Ireland	MN	Mongolia	UA	Ukraine
BR	Brazil	IL	Israel	MR	Mauritania	UG	Uganda
BY	Belarus	IS	Iceland	MW	Malawi	US	United States of America
CA	Canada	IТ	Italy	MX	Mexico	UZ	Uzbekistan
CF	Central African Republic	JP	Japan	NE	Niger	VN	Viet Nam
CG	Congo	KE	Kenya	NL	Netherlands	YU	Yugoslavia
CH	Switzerland	KG	Kyrgyzstan	NO	Norway	$\mathbf{z}\mathbf{w}$	Zimbabwe
CI	Côte d'Ivoire	KP	Democratic People's	NZ	New Zealand		
CM	Cameroon		Republic of Korea	PL	Poland		
CN	China	KR	Republic of Korea	PT	Portugal		
CU	Cuba	KZ	Kazakstan	RO	Romania		
CZ	Czech Republic	LC	Saint Lucia	RU	Russian Federation		
DE	Germany	LI	Liechtenstein	SD	Sudan		
DK	Denmark	LK	Sri Lanka	SE	Sweden		
EE	Estonia	LR	Liberia	$\mathbf{s}\mathbf{G}$	Singapore		
1							
l							

# A GEL COMPOSITION FOR SKIN CARE AND PROTECTION AND A METHOD FOR PREPARATION THEREOF

#### Field of the Invention

The present invention generally relates to a gel composition useful for skin care and protection, and to a method for its preparation. More specifically, the present invention relates to a novel liquid gel composition comprising up to 80% w/w Dead Sea water and hydrophobic or hydrophilic active agents, such as vegetable oils, free fatty acids, vitamins, humectants,  $\alpha$  - hydroxy acids, anti irritant agents, plant extracts, moisturizing agents and hydrolyzed plant proteins, or any combination thereof.

The gel composition of the present invention provides a vehicle of highly concentrated Dead Sea minerals and active agents to the skin preferably in the form of a clear gel.

#### **Background of the Invention**

The skin, which is composed of three layers differing in their cell types and special functions; an overlaying epithelial layer (epidermis), an underlying connective tissue matrix (dermis) and adipose tissue (hypodermis), is the largest organ in the body and serves as, *inter alia*, a protective barrier from the external environment, impeding the entry of microorganisms, absorption of radiation and loss of water.

Physiologists assume that specific ions from minerals play important roles, mainly in the metabolism of healthy skin, mainly as co factors in enzymatic regulation activities. For example, there are indications that Mg<sup>+2</sup> is a co factor for phosphate transferring enzymes and participates in cAMP/cATP regulation. Ca<sup>+2</sup> is thought to regulate cell membrane permeability and K<sup>+</sup> to enhance CO<sub>2</sub> transport. Also, Zn<sup>+2</sup> may participate as a co factor in cell proliferation enzymatic regulation. In some *in* vitro and *in vivo* tests magnesium bromide, magnesium chloride, and potassium

bromide exhibited inhibition of skin cell proliferation after dermal application (Ma'or Z., Magdassi S., Efron D. and Yehuda S. (1996) *Israel Journal of Medical Sciences* 32(supp.3), 28 - 35).

Minerals are capable of restoring moisture due to their hygroscopic characteristics. Minerals, if absorbed into skin cells, may enhance intracellular water capacity, and add water to the skin tissue from within.

Minerals may be absorbed into the skin from brine, from a bath with dissolved salts, or from dermal application of a mineral rich preparation. The skin is a multilayered biomembrane with certain absorption characteristics. As a dynamic living tissue, its absorption parameters are susceptible to constant changes. When applying a cosmetic blend, the most relevant parameter is the concentration cascade between each specific dissolved ion, outside and inside the skin surface. During the absorption process, a partitioning of minerals from the vehicle to skin may occur. The nature of the vehicle, namely the type of cosmetic preparation (e.g. a lipophilic cream or a hydrophilic gel), is significant in determining the kinetics of the process of skin penetration.

About 4 -5% of the human body is made up of minerals. Some skin disorders are related to a specific mineral shortage. It is assumed that specific ions from minerals play an important role in healthy skin metabolism.

The Dead Sea is the richest natural mineral source in the world, with a concentration of 32% (w/v) dissolved minerals and a unique composition.

The main elements found in Dead Sea water are chlorine, magnesium, sodium, calcium, potassium and bromine. For example, the concentration of chlorine in the Dead Sea is 224900 mg/l as opposed to 22900 in the Mediterranean and 19000 in typical ocean water. Magnesium is 44000 mg/l in the Dead Sea as opposed to 1490 and 1350 in the Mediterranean and ocean, respectively. Sodium is 40100 mg/l in the Dead Sea as opposed to 12700 and 10500 in the Mediterranean and ocean, respectively. Calcium is 17200 mg/l in the Dead Sea as opposed to 470 and 400 in the Mediterranean and ocean, respectively. Potassium is 7650 mg/l in the Dead Sea as opposed to 470 and 390 in the Mediterranean and ocean, respectively and bromine

is 5300 mg/l in the Dead Sea as opposed to 76 and 65 in the Mediterranean and ocean, respectively.

Many people, after bathing in the Dead Sea's salty water, reported a "baby smooth skin" feeling, and it is well known that minerals from the Dead Sea, as sea water, sea bath salts or sea mud have cosmetic and therapeutic effects on the skin (for example see Ma'or Z. and Yehuda S. (1997) *International Journal of Cosmetic Science* 19:105-110). However, treatment with these minerals has several drawbacks. It may be quite expensive and inconvenient for patients to travel to the Dead Sea itself for receiving treatment, and bringing the minerals to the patient's home may prove to be inconvenient. Large amounts of mineral ingredients (10kg Dead Sea mud or salts for each treatment) must be applied and the treatment may be messy (such as treatment with Dead Sea mud). Furthermore, domestic metal pipes may be corrosively attacked while taking a highly concentrated mineral bath.

Many Dead Sea cosmetic preparations sold today actually contain a very small amount of minerals due to technical difficulties in using the highly electrolyte concentrated Dead Sea solutions in cosmetic formulation and due to product stabilization.

The present invention offers a highly concentrated Dead Sea mineral gel which is a superior vehicle of minerals and hydrophobic and hydrophilic active agents that have beneficial effects on the skin, to the cosmetic preparations sold today.

The composition of the present invention has the benefits of treatment with Dead Sea minerals, but non of the drawbacks. It is easy and simple to use and in contrast with the treatments used today, may be in prolonged contact with the skin, enhancing the beneficial effects of the Dead Sea minerals.

### Summary of the invention

The present invention relates to a gel composition useful for skin care and protection comprising up to 80% w/w Dead Sea water, hydrophobic and/or hydrophilic active agents, solubilizers, gelling agents or viscosity modifiers and water to complete up to 100%. Preferably, the composition is a clear liquid gel.

In the composition of the present invention the hydrophobic active agents may be vegetable oils, free fatty acids or vitamins, or any combination thereof and the hydrophilic active agent may be humectants,  $\alpha$  - hydroxy acids, anti irritant agents, plant extracts, moisturizing agents or hydrolyzed plant proteins or any combination thereof. The gel may further comprise antioxidants and fragrances.

The present invention further relates to a method for the preparation of the said composition, comprising;

- a) heating the mixture of hydrophobic active agent and solubilizer to approximately 40°C while mixing; adding a mixture, at room temperature, of 15%w/w water and 30.0% w/w Dead Sea water, and heating again to approximately 40°C while mixing;
- b) in a different receptacle mixing the remaining water, Dead Sea water and gelling agent and heating to approximately 60°C while mixing, cooling to 40°C after receiving a clear solution;
- c) adding the product of step b) to the product of step a) while mixing, and cooling to room temperature.

According to specific requirements, a) may further copmprise a prior step of adding antioxidants and/or fragrance to the hydrophobic active agent and solubilizer, and step b) may further comprize adding the hydrophilic active agent together with the gelling agent and the remaining water and Dead Sea water.

#### Detailed description of the invention

The present invention relates to a composition comprising up to 80% Dead Sea water, hydrophobic and/or hydrophilic active agents, solubilizers and gelling agents or any viscosity modifiers for care of skin conditions, such as wrinkles, for retaining skin moisture, and for care of skin related diseases.

The nomeclature used in the present invention to describe agents and compounds used in the present compositions, is the INCI nomeclature.

Hydrophilic active agents which may be used in the composition of the present invention may be humectants, such as glycerin, glycereth - 7 or 12 or 26, butylene glycol, propylene glycol, panthenol, sorbitol and sorbitan laureth, or  $\alpha$  - hydroxy acids, such as citric acid, lactic acid, glycolic acid and malic acid or anti irritant agents, such as allantoin, PEG - 28 or PEG - 82 glyceryl tollowate or plant extracts, such as aloe barbadensis extract or gel, balm mint extract, Calendula officinalis extract, Fenugreek extract Ginseng extract, Horse chesnut extract, Ivy extract, Jujube extract, Matricaria extract and Witch hazel extract, or moisturizing agents, such as sodium hyaluronate, sodium PCA, sodium lactate, glycolipids, ceramides, sphingolipids and phospholipids and hydrolyzed plant proteins, such as hydrolyzed soy protein, hydrolyzed silk protein, hydrolyzed wheat protein, and hydrolyzed rice protein.

Hydrophobic active agents which may be used in the composition of the present invention may be vegetable oils such as avocado oil, borage oil, evening primrose oil, jojoba oil, palm kernel oil, rosehip oil, sunflower oil and wheat germ oil, or free fatty acids that are useful as moisturizers, such as ascorbic acid, linoleic acid and linolenic acid, or vitamins useful for treating skin aging effects such as ascorbyl palmitate, retinol, retinyl acetate, retinyl palmitate, retinyl propionate, tocopheryl acetate and tocopheryl linoleate.

The gelling agents which may be used in the present invention are: Guar gum, hydroxyethylcellulose, hydroxypropyl methylcellulose, methylcellulose, magnesium aluminum silicate and xanthan gum, though any appropriate viscosity modifying substance may be used.

The solubilizers used in the present invention are nonionic compounds such as tween- 20 or 80 oleth - 20, ceteth -20 and PEG-hydrogenated castor oils -36,40,60.

In the present invention the term "Dead Sea water" relates to any water with a TDS (Total Dissolved Salt) value between 25% and 40%. This value is typical for the water in the Dead Sea, and varies slightly depending on the depth and location from which the water is taken.

The composition of Dead Sea minerals is unique. The concentration of divalent cations, magnesium and calcium is very high in comparison with other sea water and the ionic strength of the solution is very high. The major constituents of Dead Sea Water referred to in the present invention, as assessed by a water analysis carried out by the Geological Survey of Israel, are:

Calcium (Ca+2) 36000 - 40000 mg/l

Chloride (Cl-) 320000 - 370000 mg/1

Magnesium (Mg+2) 90000 - 95000 mg/l

Potassium (K+) 1300 - 1500 mg/l

Sodium (Na +) 1500 - 2500 mg/l

Bromide (Br-) 11000 - 12000 mg/l

The composition of the present invention comprises Dead Sea water, hydrophobic or hydrophilic active agents, or any mixture thereof, gelling agents or any other viscosity modifiers a solubilizer and water, preferably, deionized water.

The said composition may further comprise anti oxidants and fragrances. The antioxidants may be BHA, BHT, tocopherol, tetrasodium EDTA or any combination thereof and the fragrance may be synthetic fragrances or an aromatic oil such as lavender oil, patchouli oil and sandalwood oil or any combination thereof.

The basic formula of the composition of the present invention is:

Dead Sea water	30.0 - 80.0% w/v
solubilizer	up to 4.0% w/w
hydrophilic active agent	up to 3.0% w/w
gelling agent	0.7 - 1.2% w/w
hydrophobic active agent	up to 0.8% w/w
fragrance	up to 0.4% w/w
anti oxidant	0.05 - 0.2% w/w
deionized water	up to 100% w/w

The present invention further relates to a method for the preparation of the said composition. The basic method comprises the following steps:

- a) heating the mixture of hydrophobic active agent and solubilizer to approximately 40°C while mixing; adding a mixture (at room temperature) of 15% w/w water and 30.0% w/w Dead Sea water, and heating again to approximately 40°C while mixing;
- b) in a different receptacle mixing the remaining Dead Sea water, water and gelling agent and heating to approximately 60°C while mixing, cooling to 40°C after receiving a clear solution;
- c) adding the product of step b) to the product of step a) while mixing, and cooling to room temperature.

Further additions, to the basic formula of Dead Sea water, hydrophobic active agents, solubilizer and water, according to specific requirements, comprise a prior step of adding to the above mentioned step a) anti oxidants and/or fragrances together with the hydrophobic active agent and solubilizer, and step b) further comprises adding the hydrophilic active agent together with the gelling agent (or any other viscosity modifier) and the remaining water and Dead Sea water.

The composition prepared according to this method may be used as a substitute for bath salts, and the reported "baby smooth skin" feeling when using Dead sea water is achieved without having to use large amounts of salts, and without exposing the domestic pipes to the corrosive effect of these salts. The present composition offers the added benefit of being able to "wear" the composition on the skin for many hours, thus being exposed to the benefits of the Dead Sea minerals for a longer time, enhancing their action towards skin care and protection.

The method of the present invention achieves solubilizing a hydrophobic agent in water which is highly concentrated with salts. Furthermore, the composition of the present invention is unique in that it may be a clear, transparent gel.

Transparency of the gel has important esthetic benefits; the clear transparent product may be sold in a transparent package showing off the homogeneity of the product. Also, colored active agents may be added to the gel for beauty in an encapsulated form.

Therefore, the composition of the present invention provides a superior vehicle of highly concentrated Dead Sea minerals and hydrophobic or hydrophilic active agents to the skin in the form of an esthetically superior clear gel.

The said invention will be further illustrated by the following examples. These examples do not intend to limit the scope of the invention but to demonstrate and clarify it only.

#### **Examples**

The following formulas of the peresent composition were prepared, formed a gel and were found stable for 4 weeks at 45°C. Formula I formed a clear transparent gel. (the nomeclature used in the following examples are INCI names):

Formula I	Dead Sea water	75.0% w/w	
	oleth-20	3.0% w/w	
	glycereth-26	2.0% w/w	
	hydroxyethylcellulose	0.8% w/w	
	vitamin E-acetate	٠.	
	(tocopheryl acetate)	0.3% w/w	
	lavender oil	0.3% w/w	
	ВНА	0.1% w/w	
	deionized water	up to 100%	
Formula II	Dead Sea water	50.0% w/w	
	oleth-20	2.0% w/w	
	glycerin	3.0% w/w	
	hydroxyethylcellulose	1.0% w/w	
	vitamin A-palmitate		
	(retinyl palmitate)	0.2% w/w	
	patchouli oil	0.2% w/w	
	ВНА	0.1% w/w	
	deionized water	up to 100%	
Formula III	Dead Sea water	30.0% w/w	
	oleth-20	4.0% w/w	
	glycereth-26	2.0% w/w	
	hydroxyethylcellulose	0.8% w/w	
	vitamin E acetate	0.6% w/w	
	sandalwood oil	0.2% w/w	
	BHA	0.1% w/w	
	deionized water	up to 100%	

#### **Claims**

- 1) A gel composition useful for skin care and protection comprising up to 80% w/w Dead Sea water, hydrophobic and/or hydrophilic active agents, solubilizers, gelling agents or viscosity modifiers and water to complete up to 100%.
- 2) A composition according to claim 1 wherein the composition is a clear liquid gel.
- 3) A gel composition according to claim 1 wherein the hydrophobic active agent is selected from, vegetable oils, free fatty acids and vitamins; the hydrophilic active agent is selected from humectants,  $\alpha$  hydroxy acids, anti irritant agents, plant extracts, moisturizing agents and hydrolyzed plant proteins; the solubilizer is selected from tween- 20, oleth 20, tween 80, ceteth -20 and PEG-hydrogenated castor oils -36,40 and 60 and the gelling agent or viscosity modifier is selected from Guar gum, hydroxyethylcellulose, hydroxypropyl methylcellulose, methylcellulose, magnesium aluminum silicate and xanthan gum.
- 4) A gel composition according to claim 1 wherein the water is deionized water.
- 5) A gel composition according to claim 1 further comprising antioxidants and fragrances.

6) A gel composition according to the preceding claims wherein the composition contains

Dead Sea water	30.0 - 80.0% w/w
solubilizer	up to 4.0% w/w
hydrophilic active agent	up to 3.0% w/w
gelling agent	0.7 - 1.2% w/w
hydrophobic active agent	up to 0.8% w/w
fragrance	up to 0.4% w/w
anti oxidant	0.05 <b>-</b> 0.2% w/w
deionized water	up to 100% w/w

- 7) A gel composition according to the preceding claims wherein the antioxidants are selected from BHA, BHT, tocopherol, tetrasodium EDTA and the fragrance is a synthetic fragrance or an aromatic oil selected from lavender oil, patchouli oil and sandalwood oil.
- 8) A method for the preparation of the composition according to the preceding claims, comprising;
- a) heating the mixture of hydrophobic active agent and solubilizer to approximately 40°C while mixing; adding a mixture, at room temperature, of 15%w/w water and 30.0% w/w Dead Sea water, and heating again to approximately 40°C while mixing;
- b) in a different receptacle mixing the remaining water, Dead Sea water and gelling agent and heating to approximately 60°C while mixing, cooling to 40°C after receiving a clear solution;
- c) adding the product of step b) to the product of step a) while mixing, and cooling to room temperature.

9) A method according to claim 8 wherein step a) further comprises a prior step of adding antioxidants and/or fragrance to the hydrophobic active agent and solubilizer, and step b) further comprises adding the hydrophilic active agent together with the gelling agent and the remaining water and Dead Sea water.

#### INTERNATIONAL SEARCH REPORT

Int. .tional Application No PCT/IL 98/00615

A. CLASSII IPC 6	FICATION OF SUBJECT MATTER A61K7/48 A61K7/00		
	o International Patent Classification (IPC) or to both national classification	tion and IPC	
	SEARCHED	n ourmh oto)	
IPC 6	currentation searched (classification system followed by classificatio $A61K$	,	
Documentat	tion searched other than minimum documentation to the extent that su	ich documents are included in the fields se	arched
Electronic da	ata base consulted during the international search (name of data bas	e and, where practical, search terms used)	
			,
C. DOCUME	ENTS CONSIDERED TO BE RELEVANT		
Category °	Citation of document, with indication, where appropriate, of the rele	vant passages	Relevant to claim No.
Υ	EP 0 217 975 A (BIENER, H. PROF. 15 April 1987 see column 2, line 47-55; claims		1-3
Y	FR 2 242 971 A (ELECTONIC) 4 Aprisee page 3, line 26-35; claim 1		1-3
A	PATENT ABSTRACTS OF JAPAN vol. 096, no. 008, 30 August 1996 & JP 08 104607 A (HASUNUMA KYOTARO;HANAOKA SHUSUKE), 23 Apri see abstract		1
А	EP 0 783 881 A (BEIERSDORF) 16 Ju see page 12, line 32-33; claim 1	ly 1997	1
Furt	ther documents are listed in the continuation of box C	χ Patent family members are listed	n annex.
"A" docum	ent defining the general state of the art which is not dered to be of particular relevance	"T" later document published after the inte or priority date and not in conflict with cited to understand the principle or the invention	the application but
"E" earlier document but published on or after the international filing date  "L" document of particular relevance; the cannot be considered novel or cannot be considered novel or cannot be considered novel or cannot involve an inventive step when the document which is cited to establish the publication date of another			be considered to cument is taken alone
citation or other special reason (as specified)  "O" document referring to an oral disclosure, use, exhibition or other means  "O" document referring to an oral disclosure, use, exhibition or other means  "O" document is combined with one or more other such document is combined with one or more other such document is combined with one or more other such document is combined with one or more other such document is combined with one or more other such document is combined with one or more other such document.			
"P" docum later t	ent published prior to the international filing date but than the priority date claimed	in the art. "&" document member of the same patent	family
	actual completion of the international search	Date of mailing of the international sea	arch report
2	20 April 1999	27/04/1999	
Name and	mailing address of the ISA European Patent Office, P.B. 5818 Patentiaan 2	Authorized officer	
	NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Beyss, E	

1

# INTERNATIONAL SEARCH REPORT information on patent family members

tional Application No. PCT/IL 98/00615

Patent document cited in search repo	rt	Publication date	Patent family member(s)	Publication date
EP 217975	Α	15-04-1987	AT 69954 T CA 1283853 A US 4943432 A	15-12-1991 07-05-1991 24-07-1990
FR 2242971	Α	04-04-1975	NONE	
EP 783881	Α	16-07-1997	DE 19548015 A JP 9175973 A	26-06-1997 08-07-1997